DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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ALERE SCARBOROUGH, INC
ANGELA DRYSDALE
VP, REGULATORY & CLINICAL AFFAIRS
10 SOUTHGATE ROAD
SCARBOROUGH ME 04074

March 31, 2015

Re: K141757
Trade/Device Name: Alere i Strep A
Regulation Number: 21 CFR 866.2680
Regulation Name: Streptococcus spp. Nucleic Acid-Based Assay
Regulatory Class: II
Product Code: PGX, OOI
Dated: March 9, 2015
Received: March 10, 2015

Dear Ms. Drysdale:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Uwe Scherf -S for

Sally Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K141757

Device Name
Alere™ i Strep A

Indications for Use *(Describe)*

Alere™ i Strep A is a rapid, instrument-based, molecular in vitro diagnostic test utilizing isothermal nucleic acid amplification technology for the qualitative detection of Streptococcus pyogenes, Group A Streptococcus bacterial nucleic acid in throat swab specimens obtained from patients with signs and symptoms of pharyngitis. It is intended to aid in the rapid diagnosis of Group A Streptococcus bacterial infections.

All negative test results should be confirmed by bacterial culture because negative results do not preclude infection with Group A Streptococcus and should not be used as the sole basis for treatment.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(K) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K141757

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DATE PREPARED
3/26/2015

TRADE NAME
Alere™ i Strep A

COMMON NAME
Alere™ i Strep, Alere™ i, Alere™ Strep A

CLASSIFICATION NAME
Groups A, C and G Beta Hemolytic *Streptococcus* Nucleic acid Amplification System (per 21 CFR 866.2680)
Real Time Nucleic Acid Amplification System (per 21 CFR 862.2570)

CLASSIFICATION
Class II

PRODUCT CODE
PGX, OOI

PANEL
Microbiology (83)

PREDICATE DEVICE
Lyra Direct Strep Assay, K133883

DEVICE DESCRIPTION

Alere™ i Strep A is a rapid, instrument-based isothermal test for the qualitative detection of Group A Strep from throat swab specimens. The **Alere™ i** Strep A System utilizes isothermal nucleic acid amplification technology and is comprised of:

- Sample Receiver – single use, disposable containing the elution buffer
- Test Base – single use, disposable comprising two sealed reaction tubes, each containing a lyophilized pellet
- Transfer Cartridge – single use, disposable for transfer of the eluted sample to the Test Base, and
- **Alere™ i** Instrument – repeat use reader

The reaction tubes in the Test Base contain the reagents required for Group A Strep bacterial lysis and the subsequent amplification of the target nucleic acid and an internal control. **Alere™ i** Strep A utilizes a pair of templates (similar to primers) for the specific amplification of DNA from Group A Strep and a fluorescently labeled molecular beacon designed to specifically identify the amplified nucleic acid target. **Alere™ i** Strep A is performed within the confinement of the Test Base, and no other part of the **Alere™ i** Instrument has contact with the sample during the amplification process. This reduces the risk of instrument contamination and sample carry-over between measurements.

To perform the assay, the Sample Receiver and Test Base are inserted into the **Alere™ i** Instrument and the elution buffer is automatically heated by the instrument. The sample is added to the Sample Receiver and transferred via the Transfer Cartridge to the Test Base, resuspending the lyophilized pellets contained within the Test Base and initiating bacterial lysis and target amplification. Heating, mixing and detection by fluorescence is provided by the instrument, with results automatically reported.

Results are displayed by the **Alere™ i** Instrument and are also stored in an on-board archive and are assigned to a sample ID that has been entered into the **Alere™ i** Instrument by the operator, and the date/time the test was performed. Data can be retrieved and downloaded by the operator at any time after testing. An external Alere™ Universal Printer can be attached via USB to the **Alere™ i** Instrument to print test results.

INTENDED USE

Alere™ i Strep A is a rapid, instrument-based, molecular *in vitro* diagnostic test utilizing isothermal nucleic acid amplification technology for the qualitative detection of *Streptococcus pyogenes,* Group A *Streptococcus* bacterial nucleic acid in throat swab specimens obtained from patients with signs and symptoms of pharyngitis. It is intended to aid in the rapid diagnosis of Group A *Streptococcus* bacterial infections.

All negative test results should be confirmed by bacterial culture because negative results do not preclude infection with Group A *Streptococcus* and should not be used as the sole basis for treatment.

TECHNOLOGICAL CHARACTERISTICS

Alere™ i Strep A and the predicate device, Lyra Direct Strep Assay, have the same intended use, indications for use, and utilize similar basic principles of operation. They are both molecular tests for the qualitative detection of Group A Strep nucleic acid.

DEVICE COMPARISON

Alere™ i Strep A was compared to the legally marketed predicate device, the Lyra Direct Strep Assay.

Parameter	Alere™ i Strep A	Lyra Direct Strep Assay (K133883)
FDA Product Code	PGX, OOI	Same
Assay Target	*Streptococcus pyogenes*	*Streptococcus pyogenes* , pyogenic Group C and G β-hemolytic *Streptococcus*
Intended Use	**Alere™ i** Strep A is a rapid, instrument-based, molecular *in vitro* diagnostic test utilizing isothermal nucleic acid amplification technology for the qualitative detection of *Streptococcus pyogenes*, Group A *Streptococcus* bacterial nucleic acid in throat swab specimens obtained from patients with signs and symptoms of pharyngitis. It is intended to aid in the rapid diagnosis of Group A *Streptococcus* bacterial infections. All negative test results should be confirmed by bacterial culture because negative results do not preclude infection with Group A *Streptococcus* and should not be used as the sole basis for treatment,	The Lyra Direct Strep Assay is a Real-Time PCR *in vitro* diagnostic test for the qualitative detection and differentiation of Group A β-hemolytic *Streptococcus* (*Streptococcus pyogenes*) and pyogenic Group C and G β-hemolytic *Streptococcus* nucleic acids isolated from throat swab specimens obtained from patients with signs and symptoms of pharyngitis, such as sore throat. The assay does not differentiate between pyogenic Groups C and G β-hemolytic *Streptococcus*. All negative test results should be confirmed by bacterial culture, because negative results do not preclude Group A, C or G Strep infection and should not be used as the sole basis for treatment. The assay is intended for use in hospital, reference, or state laboratory settings. The device is not intended for point-of-care use.
Instrumentation	**Alere™ i** Instrument	ABI 7500 Fast DX Thermocycler
Assay Information		
Sample Type	Throat Swab	Same
Target Analyte	Group A *Streptococcus* (*Streptococcus pyogenes*)	Group A *Streptococcus* (*Streptococcus pyogenes*) Groups C and G *Streptococcus*
Technology	Isothermal nucleic acid amplification	Multiplex Real-time PCR
Internal Control	Yes	Same
Result Interpretation	Automated	Same
Assay Result	Qualitative	Same
Time to Result	< 8 minutes	<70 minutes after extraction

PERFORMANCE SUMMARY

CLINICAL STUDY

The clinical performance of **Alere™ i** Strep A was established in a multi-center, prospective clinical study conducted at 8 US trial sites in 2014.

A total of 481 evaluable throat swab specimens, collected from patients of all ages presenting with symptoms of pharyngitis, were evaluated with **Alere™ i** Strep A, and compared to bacterial culture. Sixty-two percent (62%) of the population tested was female and 38% was male.

In this study, two (2) throat swabs were collected from each of a total of 481 patients. One throat swab from each patient was tested with **Alere™ i** Strep A. The other throat swab was sent to a laboratory for bacterial culture.

Alere™ i Strep A performance, including 95% confidence intervals, versus bacterial culture is provided below.

Alere™ i Strep A Performance vs. Culture (All Age Groups Combined)

	Culture +	**Culture -**	
Alere™ i +	141	18[a]	159
Alere™ i -	6[b]	316	322
	147	334	481

Sensitivity: 141/147 = 95.9% (95% CI = 91.4%, 98.1%)
Specificity: 316/334 = 94.6% (95% CI = 91.6%, 96.6%)
Positive Predictive Value = 141/159 = 88.7% (82.8%, 92.7%
Negative Predictive Value = 316/322 = 98.1% (96.0%, 99.1%)

[a] Of the 18 samples positive by **Alere™ i** Strep A and negative by bacterial culture, 13 were also positive for Group A Strep by a laboratory developed real-time PCR assay and [b] of the 6 samples negative by **Alere™ i** Strep A and positive by bacterial culture, 4 samples were also negative for Group A Strep by a laboratory developed real-time PCR assay.

During the prospective clinical study, the initial invalid rate (before repeat testing per the product instructions) was 4.8% (24/495) (95% CI: 3.3%, 7.1%). After repeat testing per the product instructions, the invalid rate was 2.8% (14/495) (95% CI: 1.7%, 4.8%).

ANALYTICAL STUDIES

ANALYTICAL SENSITIVITY

Alere™ i Strep A limit of detection (LOD or C_{95}), defined as the concentration of Group A strep bacteria that produces positive **Alere™ i** Strep A results approximately 95% of the time, was identified by evaluating different concentrations of 2 strains of Group A Strep in **Alere™ i** Strep A . The concentrations identified as the LOD (or C_{95}) levels for each strain tested are listed below.

Group A Strep Strain	**Concentration (CFU/mL of Elution Buffer)**	**# Detected per Total Tests**	**% Detected**
ATCC 12344	4.2	19/20	95%
ATCC 19615	41.8	19/20	95%

REACTIVITY TESTING

The following Group A Strep strains were tested and produced positive results at or near the stated assay limit of detection of the **Alere™ i** Strep A test: ATCC8135, ATCC12384, ATCC12202, ATCC12203, ATCC12204, ATCC12365, ATCC14289, ATCC49399, ATCC51339, ATCC700294, ATCC12357, ATCC12385 (Loomis), ATCC 12385 (Type 4).

ANALYTICAL SPECIFICITY (CROSS-REACTIVITY)

To determine the analytical specificity of **Alere™ i** Strep A, 33 commensal and pathogenic microorganisms (32 bacteria and 1 yeast) that may be present in the throat were tested. All of the following microorganisms and yeast produced negative results when tested at concentrations ranging from 10^6 to 10^9 cells/mL of Elution Buffer.

Bacteria	**Yeast**
Arcanobacterium haemolyticum[1]	*Candida albicans*
Bacillus cereus	
Bordetella pertussis	
Burkholderia cepacia	
Campylobacter rectus	
Corynebacterium diphtheria	
Enterococcus faecalis	
Escherichia coli	
Fusobacterium necrophorum	
Haemophilus influenzae	
Klebsiella pneumoniae	
Lactobacillus acidophilus	
Moraxella catarrhalis[1,2]	
Neisseria gonorrhoeae	
Peptostreptococcus micros	
Prevotella (Bacteroides) oralis[1]	
Pseudomonas aeruginosa	
Staphylococcus aureus	
Staphylococcus epidermidis	
Streptococcus agalactiae	
Streptococcus aginosus	
Streptococcus canis	
Streptococcus dysgalactiae subsp equisimilis	
Streptococcus gallolyticus	
Streptococcus intermedius	
Streptococcus mitis	
Streptococcus mutans	
Streptococcus pneumoniae	
Streptococcus salivarius	
Streptococcus sanguinis	
Treponema denticola	
Veillonella parvula	

[1]Invalid results obtained at $\geq 10^6$ cells/mL of Elution Buffer
[2]One false-positive result obtained a $>10^8$ cells/mL of Elution Buffer

INTERFERING SUBSTANCES

The following substances, naturally present in throat swab specimens or that may be artificially introduced into the throat, were evaluated with **Alere™ i** Strep A at the concentrations listed below and were found not to affect test performance.

Substance	Concentration
Whole Blood	5% (v/v)
Mucin	0.016% (w/v)
Human Saliva	10% (v/v)
Ibuprophen	15.4 mg/mL
Acetaminophen	19.4 mg/mL
Acetylsalicylic acid	12.4 mg/mL
Albuterol	0.5 mg/mL
Diphenhydramine HCL	2.7 mg/mL
Cepacol® Sore Throat Lozenges - cherry	20% (w/v)
Sucrets® Sore Throat & Cough - cherry	20% (w/v)
Halls Plus® – Honey Lemon	20% (w/v)
ACT® Total Care – Fresh Mint	20% (v/v)
Cepacol® Mouthwash	20% (v/v)
Listerine® Antiseptic Mouthwash - Original	20% (v/v)
Crest® Complete Multi-Benefit Whitening + Deep Clean Toothpaste	0.16% (w/v)
Zicam® Oral Mist – arctic mint	20% (v/v)
Chloraseptic® Max Sore Throat Relief + Coating Action – wild berry	20% (v/v)
Contact Cold & Flu Tablets - Night	20% (w/v)
Robitussin® Maximum Strength Nighttime Cough DM	20% (v/v)
Tylenol® Cold Multi-Symptom Liquid	20% (v/v)
Children's Dimetapp® Cough & Cold	20% (v/v)

When Mucin was tested at a concentration of 2%, 0.4%, and 0.08%, false negative results were observed.

When Crest® Complete Multi-Benefit Whitening + Deep Clean Toothpaste were tested at 20% and 4% invalid results were observed. Additionally, false negative results were observed when tested at a concentration of 0.8%.

REPRODUCIBILITY

A reproducibility study of **Alere™ i** Strep A was conducted by operators from 3 sites using panels of blind coded specimens containing negative, high negative (below the limit of detection), low positive (~3X limit of detection), and moderate positive (~19X the limit of detection) Group A Strep bacterial samples. Participants tested multiple samples of each panel member on 5 different days. The percent agreement with expected results for the Strep A moderate positive and low positive samples were 100% (90/90) and 91.1% (82/90). All of the negative samples (90) generated negative test results as did 94.4% (85/90) high negative samples. There were a total of 5 invalid results on initial testing (5/360 samples; 1.4%). There were no significant differences within run (replicates tested by one operator), between run (5 different days), between sites (3 sites), or between operators (6 operators).

The results of the analytical and clinical studies performed with Alere™ i Strep A support the determination of substantial equivalence in accordance with the stated intended use and device labeling.